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EXAMINER	
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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Paper No. 34

Application Number: 08/300,510
Filing Date: 09/02/94
Appellant(s): Gefter et al.

Jeanne M. DiGiorgio
For Appellant

EXAMINER'S ANSWER

This is in response to appellant's brief on appeal filed 10/29/98.

(1) Real Party in Interest

A statement identifying the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The brief does not contain a statement identifying the related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief. Therefore, it is presumed that there are none. The Board, however, may exercise its discretion to require an explicit statement as to the existence of any related appeals and interferences.

(3) Status of Claims

The statement of the status of the claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Invention

The summary of invention contained in the brief is correct. Applicant's election without traverse of the species of method comprising administration of a peptide comprising a T cell epitope recognized by a T cell receptor specific for the protein allergen of the genus Felis, Fel d I and subcutaneous administration of said peptide in Paper No. 20 is acknowledged. The elected species is a method of treating allergy in humans comprising subcutaneous administration over a period of no more than six weeks, three to six doses of a peptide less than 50 amino acid residues derived from the Fel d I protein allergen.

Claims 103-144 as they encompass the use of structurally distinct peptides from other allergens or on nonsubcutaneous modes of administration are withdrawn from further consideration by the examiner, 37 CFR 1.142(b) as being drawn to a non-elected species. Election was made **without** traverse in Paper No. 20.

(6) Issues

The appellant's statement of the issues in the brief is correct. The Examiner reiterates that these issues have been considered only in regard to the elected species of peptide: Fel d I.

(7) Grouping of Claims

Appellant's brief includes a statement that the rejected claims do not stand or fall together (see page 10, sentence above section VIII) but does not provide reasons as set forth in 37 CFR 1.192(c)(7) and (c)(8). Therefore, claims grouped under the same ground of

rejection are presumed to stand or fall together only for the purposes of that particular rejection.

(8) Claims Appealed

The copy of the appealed claims contained in the Appendix to the brief is correct.

(9) Prior Art of Record

The following is a listing of the prior art of record relied upon in the rejection of claims under appeal.

Sehon, A. H. Et al., "Suppression of immunoglobulin E antibodies with modified allergens", J. Allergy Clin. Immunol., vol. 64, (1979), pp. 242-250.

Litwin, A. Et al., "Regulation of the human immune response to ragweed pollen by immunotherapy. A controlled trial comparing the effect of immunosuppressive peptic fragments of short ragweed with standard treatment", Clin. Exp. Allergy, vol. 21 (1991), pp. 457-465.

5,328,991	Kuo	July 12, 1994
4,338,297	Michael et al.	July 6, 1982

(10) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Rejection under 35 U.S.C. 112, second paragraph

Claim 133 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 133 it is unclear what the metes and bounds of the term "nonimmunogenic" are. The administration of the claimed products and compositions appears to result in a down regulation of the immune system. Does "non-immunogenic" refer to the inability of a particular composition to induce an antibody or cellular immune response? Does this mean that the claimed compositions are also incapable of inducing suppressor T cells, or other suppressive immune phenomena such as high or low zone tolerance, which would be expected to down-regulate antigen-specific immune responses?

--Appellant's arguments have been considered and would be persuasive upon entry of the proposed amendment limiting the claimed compositions to those without adjuvant. The term "non-immunogenic" is problematic in part because the prior art tolerization methods (cited

below) refer to induction of T-suppressor cells using tolerogenic peptides. Such induction could be considered to render peptides bearing T cell epitopes immunogenic. The prior art also addresses maintaining T cell epitopes while diminishing humoral immune responses. Thus, the issue of which type of "non-immunogenicity" is encompassed by the claims was raised. This proposed claim language limitation was not entered because while it obviates the issue under 35 U.S.C. 112, second paragraph it raises new search and scope of enablement issues.

Rejection under 35 U.S.C. 112, first paragraph

A. Claim 133 and claims 103-144 as they encompass use of nonimmunogenic peptides are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The peptides used in the claimed methods are "immunogenic" as they induce immune responses in human patients, see e.g. page 23, line 26 of the specification. Thus, the claim limitation in claim 133 to use of "nonimmunogenic" peptides is not adequately supported. Perhaps an alternative term such as "tolerogenic" would be better supported.

--Appellant's arguments have been considered and would be persuasive upon entry of the proposed amendment limiting the claimed compositions to those without adjuvant. This proposed claim language limitation was not entered because while it obviates some issues

under 35 U.S.C. 112, first paragraph it would raise new search and scope of enablement issues.

Rejection under 35 U.S.C. 103(a)

B. Claims 103-144 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Sehon et al., J. Allergy Clin. Immunol. 64:242-250 (1979), Michael et al, U.S. patent 4,338,297 (issued 1982) or Litwin et al., Clin. Exp. Allergy 21:457-465 (1991) in view of Kuo et al., U.S. patent 5,328,991 (filed 1991). The claims are drawn to methods comprising the subcutaneous therapeutic use of at least one peptide comprising less than 50 residues and containing at least one T cell epitope of the Fel d I antigen.

Sehon et al. teach a variety of methods of making tolerogens from allergens and using such tolerogens to induce tolerance to particular allergens. Michael et al. teach how to make and use proteolytic fragments of pollen allergens to desensitize subjects to allergy. Litwin et al. teach how to make and use immunosuppressive peptide fragments of allergens to treat allergy. Kuo et al., see abstract and claims, teach modified Fel d I antigen and its use for inducing tolerance in patients allergic to cat cats.

It would have been prima facie obvious to one of ordinary skill in the art at the time of invention to substitute the Fel d I peptides (or fragments of the Fel d I peptides) taught by Kuo et al. into the tolerization or antigenic desensitization methods taught by the cited references order to induce tolerance or anergy in patients exposed to the Fel d I allergen. Routine

optimization of the dosage and mode of administration of the instant compositions fall within the ordinary skill of the art as evidenced by the cited references, see e.g. Litwin et al. page 457, first column who refer to "repeated subcutaneous injections" and methods of determining appropriate protocols for therapeutic administration of tolerogens. See also, cols. 1-6 of Michael et al. who refer to subcutaneous injections of peptide tolerogens and methods of monitoring safety and efficacy of such injections. Page 242 of Sehon et al. also teach administration of a series of injections of the offending allergen. Thus, claims 103-144 are prima facie obvious over the cited prior art.

(11) Response to Argument

C. The Examiner agrees with the Appellant's comments on pages 14-15 of the Brief that the Sehon et al., Michael et al., and Litwin et al. references do not teach Fel d I allergen, fragments of this allergen or its amino acid sequence. These reference provide motivation and teachings about how to make tolerogens in general, but do not teach the specific tolerogen Fel d I. However, Kuo et al. teach all of these aspects of Fel d I.

Appellant urges that Kuo et al. "Merely teaches whole Fel d I protein modified by treatment with mild base or alkali conditions to reduce IgE reactivity", see page 16 of the Brief. This is not entirely correct as Figs. 1a and 1b of Kuo et al. teach the defined amino acid sequences of each of the Fel d I (also known as TRFP) chains. See col. 3 lines 26-29 which indicate that the first chain is a 70 amino acid peptide and that the second chain occurs as either a 92 or 90 residue peptide. Col. 4 indicates that Fel d I (TRFP) may be chemically synthesized or produced by recombinant DNA techniques, see lines 14-15 and 21.

The instant open claim language (e.g. comprises less than 50 amino acid residues) has been interpreted as imposing no definite limitation on the lengths of the recited Fel d I peptides, particularly in view of the commentary on page 14 of the Brief which suggests that the instant peptides are unconjugated. Thus, any of the three different Fel d I chains disclosed by Kuo et al. would read on the instantly recited peptides. Assuming arguendo that it is Appellant's intent to limit the elected species to peptides consisting of 50 or fewer residues

from the Fel d I antigen, then one with ordinary skill in the art would have still have been motivated by Kuo et al., col. 6, lines 28-34 and 66-68 and col. 7, lines 38-50 to select fragments of the known Fel d I that had T cell epitopes but lacked IgE reactive portions of Fel d I and enabled to screen such fragments for tolerogenic activity based on the assays taught by the other cited prior art.

Appellant urges on pages 14-15 of the Brief that the prior art does not provide motivation for use of peptides containing T cell epitopes. However, Kuo et al., col. 6, lines 28-33 discloses the importance of selecting Fel d I peptides retaining T cell reactive structures (i.e. T cell epitopes).

Appellant urges that the instant purity limitations such as "purified to at least 90%" distinguish the instant compositions from those of the prior art. However, the instant claims are not limited to compositions comprising a single peptide, but can read on mixtures of tolerogenic peptides, see e.g. independent claim 103: "at least one". Kuo et al. teaches the advantage of affinity purification of the Fel d I antigen to purify it away from other substances in poorly-defined animal dander extract, see e.g. col. 2, lines 14-17. The disclosure of Kuo et al. is directed to use of purified Fel d I peptides, poorly-defined animal dander extracts are not used.

D. Appellant urges that claims 104, 106, 109, 111, 113, 120, and 121 as directed to peptides "comprising 50 amino acid residues or less" are not suggested by the cited prior art. One with

ordinary skill in the art would have been enabled to identify active peptide fragments of the Fel d I allergen based on the teachings of the cited prior art.

E. Appellant urges that claims 105, 127, 134-137 as directed to peptide compositions in certain dosage ranges not suggested by the prior art. These claims recite dosages within the ranges of 20ug-1.5mg per kg body weight. One with ordinary skill in the art at the time of invention would have been enabled to optimize peptide dosage ranges based on the assays taught by the cited prior art.

F. Appellant urges that claims 107 and 124-126 are directed to compositions which specify a mean T cell stimulation index not suggested by the prior art. The prior art is silent with regard to the degree of T cell stimulation that would be provided by administration of Fel d I peptides. However, it clearly suggests the utility of preserving T cell epitopes on Fel d I peptides. One with ordinary skill in the art at the time of invention would have been motivated to select Fel d I peptides that provide maximal T cell stimulation based on the teachings of Kuo et al. that Fel d I peptides retain T cell reactive structures, see col. 6 lines 28-34.

G. Appellant urges that claims 115-119 are directed to compositions that comprise peptides with different degrees of purity, e.g. 90%, 95%, or 97% not suggested by the cited prior art.

Kuo et al. teach affinity purification of the Fel d I antigen. Affinity purified Fel d I would be expected to be close to 100% pure Fel d I. Kuo et al. also provide motivation for isolating individual antigenic peptides from undefined allergenic extracts and disclose recombinant DNA and protein synthesis methods useful for producing peptides at the purity levels recited by claims 115-119.

H. Appellant urges that claims 122-123 are directed to compositions in which the protein allegen is selected from a designated protein allegen species. The elected species of peptide is directed to Fel d I , therefore this issue has already been considered above as claims 122-123 have been examined to the extent that they read on the elected species.

I. Appellant urges that claims 138-144 are directed to methods of treatment using compositions that result in statistically-significant improvement as compared to a placebo, not taught by the cited prior art. While the cited prior art is silent with respect to the degree of improvement measured using the assays set forth by the instant disclosure, use of the prior art Fel d I peptides or fragments of the Fel d I allergen that comprise T cell epitopes would reasonably be expected to provide therapeutic benefit within the ranges recited by claims 138-144 as immune responses, nasal symptoms and lung systems are all aspects of an allergic response to cat antigens such as Fel d I.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

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January 19, 1999

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